525 Rec'd PCT/PTO 08 DEC 2000

FORM PTO-1390 (REV 10-94) U.S. Dept. of Commerce and Patent and Trademark Office

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: **H01.2-9587**

U.S. APPLICATION NO. (If known): **09/719258**

INTERNATIONAL APPLICATION NO.:	INTERNATIONAL FILING DATE (dd/mm/yy):	PRIORITY DATE CLAIMED (dd/mm/yy):
PCT/EP00/03350	**13 April 2000**	**30 June 1999**

TITLE OF INVENTION:
ORAL DOSAGE FORM

APPLICANT(S) FOR DO/EO/US:
Friedel Frauendorfer

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.

2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.

3. ☒ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).

4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.

5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☐ is transmitted herewith (required only if not transmitted by the International bureau).
   b. ☒ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States receiving Office (RO/US).

6. ☒ A translation of the International Application into English (35 U.S.C. 371 (c)(2)).

7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☒ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☐ have not been made and will not be made.

8. ☒ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).

9. ☒ An oath or declaration of the inventor (35 U.S.C. 371(c)(4)).

10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.

12. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.29 and 3.31 is included.

13. ☒ A **FIRST** preliminary amendment. Please enter the amendment before fee calculation.
    ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.

14. ☐ A substitute specification.

15. ☐ A change of power of attorney and/or address letter.

16. ☒ Other items or information: Power of Attorney; Construction Petition; Correspondence Address document; Verified Statement Claiming Small Entity.

17. ☒ The following fees are submitted:	CALCULATIONS	PTO USE ONLY
BASIC NATIONAL FEE (37 CFR 1.492(A)(1)-(5)): *(select the appropriate one of the following fees)* Search Report has been prepared by the EPO or JPO ..... $ 930.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) ..... $ 490.00 No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) ..... $ 750.00 Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO ..... $ 1,070.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Articles 33(2)-33(4) ..... $ 98.00 **ENTER APPROPRIATE BASIC FEE AMOUNT =**	$930.00	
Surcharge of $130.00 for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total Claims	10- 20 =		x $ 22.00	$	
Independent Claims	1 - 3 =	0	x $ 82.00	$	
Multiple Dependent Claims (if applicable)			+ $ 270.00	$	
		TOTAL OF ABOVE CALCULATIONS =		$930.00	
Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must be filed also. (Note 37 CFR 1.9, 1.27, 1.28).				$	
		SUBTOTAL =		$465.00	
Processing fee of $130.00 for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				$	
		TOTAL NATIONAL FEE =		$	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40.00 per property				$40.00	
		TOTAL FEES ENCLOSED =		$505.00	
				Amount to be: Refunded	$
				Charged	$

a. ☒ A check in the amount of $505.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of $_____ to cover the above fees is enclosed. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 22-0350.

Send All Correspondence To:
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By: _____
RICHARD A. ARRETT, ESQ.
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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
UNITED STATES RECEIVING OFFICE (RO/US)

In re Application of:	Friedel Frauendorfer
U.S. Nat'l Stage of Int'l App. No.:	PCT/EP00/03350
Int'l Filing Date:	13 April 2000
For:	ORAL DOSAGE FORM

Box PCT
ATTN: EO/US
Assistant Commissioner for Patents
Washington, D.C. 20231

Docket No.: H01.2-9587

PRELIMINARY AMENDMENT

Dear Sir:

Before calculating the filing fee please enter the following amendments.

In The Claims:

Claim 3, line 1, delete "or 2";

Claim 4, line l, delete "one of claims 1 to 3" and insert -- claim l --;

Claim 5, line l, delete "one of the preceding claims" and insert -- claim 1 --;

Claim 9, line l, delete "one of claims 6 to 8" and insert -- claim 6 --;

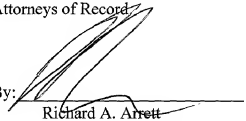
Claim 10, line l, delete "one of claims 6 to 9" and insert -- claim 6 --;

REMARKS

The claim amendments are being made to remove the multiply dependent claim.

Respectfully submitted,

Vidas, Arrett & Steinkraus, P.A.
Attorneys of Record



By: Richard A. Arrett
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Dated: November 29, 2000
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PATENT/DESIGN PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor: Friedel Frauendorfer

Title: ORAL DOSAGE FORM

Filed: [x] Concurrently herewith
[ ] on _____
Ser. No. _____

VERIFIED STATEMENT CLAIMING SMALL ENTITY STATUS

(ASSIGNEE FORM)

Docket No. H01-9597

As a representative of the below named company I hereby state that:

1.I am empowered to act on behalf of the Company in making the following statements to establish status as a small entity under 37 C.F.R. § 1.9.

2. By assignment of all right, title and interest in and to the invention described above, the Company is the owner of the subject matter of a patent application identified above, the docket no., filing date and application number of which application may be inserted above by any attorney of Vidas, Arrett & Steinkraus, P.A., when known.

3. The company has not assigned, granted, conveyed or licensed any rights in and to the invention, and is not under any obligation, contract or law to assign, grant, convey or license any rights to said invention to any other party.

4. The Company is a business concern which presently employs less than 500 persons.

5. Based upon the above facts, it is believed that the Company is a Small Business for paying reduced fees as set forth in 37 C.F.R. §1.9(d).

6. The company acknowledges its duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate (37 C.F.R. §1.28(b)).

7. The Company hereby declares that all statements made herein of its own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Meduna Arzneimittel GmbH
Company name

Ernst-Grote-Strasse 23, D-30916 Isernhagen/Germany
Company address

Dated: 20th November 2000

By _____
Friedel Frauendorfer

Title Managing Director

(Filing date, serial number and docket number may be left blank at time of signing)

VIDAS, ARRETT & STEINKRAUS
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Oral Dosage Form

The present invention relates to an oral dosage form for food, food supplement, and dietetics.

In the field of food supplement, dietetics and drugs the use of omega-3 polyunsaturated acids is known. Fish oil, linseed oil, cod-liver oil or the like is used to provide said polyunsaturated acids. It is known to supply said substances in gelatine capsules to control the unpleasant taste and to avoid flatulences. To reduce the risk of rapid oxidation and thereby the risk of enlarged toxicity, the oil is mixed with antioxidants. Rapid oxidation (becoming rancid) causes not only the development of unhealthy radicals but also reduces the durability of the products. A further problem is the risk that polyunsaturated acids are subject to undesired changes in the stomach and in the duodenum before they enter the small intestine, whereby said acids are not or only partly available in the location of resorption.

WO90/04391 discloses an oral dosage form of omega-3 polyunsaturated acids to overcome the problems of vascular diseases. It is known to supply said acids in soft gelatine capsule shells. WO96/36329 discloses to provide gelatine capsules with a coat of poly ethyl acrylate-methyl-methacrylate. The coat prevents releasing of acid from the capsule already in the stomach.

A pure gelatine capsule prevents neither the risk of changes in the structure of the polyunsaturated acids nor undesired flatulences together with its unpleasant smell.

.../2

EP 2 240 581 B1 discloses a gelatine capsule for pharmaceutical use with a controlled release of active ingredients and a process for the preparation of said gelatine capsules. During said process xylose is added to the liquid gelatine from which afterwards gelatine capsules are formed. Gelatine capsules manufactured according to the process provide retarded release of active ingredients.

The underlying problem of the invention is to provide an oral dosage form for polyunsaturated acids comprising food, food supplement, and dietetics which provides a longer durability for the polyunsaturated acids. Furthermore, the oral dosage form should be admissible under food regulations.

The problem is solved with the features of claim 1.

According to the present invention, polyunsaturated acids are provided in gelatine capsules. The gelatine capsule is hardened with the help of xylose. The hardening provides a retarded opening time of the capsule from about 45 minutes and more.

Typically fatty acids are mixed with antioxidants such as tocopherole, ascorbylpalmitate, propyl gallate and the like. The addition of antioxidants is avoided according to the invention because the xylose hardening prevents fat from "going bad". The peroxidation of the unsaturated acids is an important reaction for going bad of fat. Surprisingly, the dosage form according to the invention provides a low peroxidation, and a considerable delay in time for the fat to become rancid.

The oral dosage form according to the invention provides an undisturbed release of polyunsaturated acids in the intestine after passing the stomach. An unpleasant smell and flatulences are prevented.

Xylose is a well-known adjuvant in food industry which is inter alia re-claimable waste of the cellulose production. Xylose is also suitable as sweetening agent. Furthermore, xylose has a laxative effect.

Omega-3 polyunsaturated acids with a high content of alpha linolenic acid, preferred perilla oil, can be used as polyunsaturated fatty acids. Also the use of fish oil, linseed oil, and gamma-linolenic acid is preferred.

The dosage form according to the invention is very well suited for essential fatty acids of all kinds which are delicate to formation of toxic radicals. For the use of the dosage form the following requirements hold:

- peroxide value < 2,
- no advanced decomposition in the stomach or in the duodenum,
- resorption in the small intestine.

Surprisingly all these requirements are achieved with the dosage form according to the invention.

According to a preferred embodiment of the invention the gelatine capsule is filled with perilla oil. Perilla oil is gained from the oil-containing fruits of the Asian plant perilla fructuence. The perilla oil contains more than 70% of unsaturated fatty acids, in particular α-linolenic acid.

A plurality of scientific studies has proven positive effects for the metabolism of fat (metabolic syndrome) and an antiphlogistic effect in the intestine (Morbus Crohn). Perilla oil has furthermore the advantage of being almost without taste and smell.

Two galenic forms, a pure gelatine capsule and a xylose-hardened capsule, each containing perilla oil, have been tested for their peroxide value at 20°C and 45% humidity for a time period of 12 months. The peroxide value of the xylose-hardened capsule was significantly lower than that of the pure gelatine capsule and did not increase during the testing period but even decreased.

In the study 24 persons took 3 to 6 capsules à 500 mg perilla oil over 4 weeks, no nausea, no stomach pressure, or other symptoms were observed. The persons' ability to taste was not reduced.

Example:

500 mg perilla oil capsule without xylose hardening during the long term test:

	0 Months	3 Months	6 Months	12 Months
Perilla Oil / Perilla Oil mg	498.2	506.2	513.5	486.1
Perilla Oil / α-Linolenic Acid mg	260	264.2	268	253.7
Peroxide Value	2.3	2.5	3.1	3

500 mg perilla oil capsule with xylose hardening during the long term test:

	0 Months	3 Months	6 Months	12 Months
Perilla Oil / Perilla Oil mg	498.7	508.1	513.8	489.2
Perilla Oil / α-Linolenic Acid mg	260.3	265.2	268.2	255.5
Peroxide Value	2.1	2.1	1.6	1

Blister packaging was used during the long term test.

Xylose hardening can be achieved according to EP 0 240 581 B1, especially according to Example 3 of the specification. In an alternative approach it is possible to uniformly spray the capsule with a solution comprising xylose, ethanol and water for a predetermined time interval. During this time the capsules are heated. After spraying a predetermined amount of hardening solution, the capsules are heat-treated for a predetermined time interval. The heat treatment causes the aldehyd function of the xylose to react with the gelatine and to provide a cross-linking. The cross-linking causes the hardening of the gelatine capsule. The finished product provides a structure which inhibits the peroxidation of fatty acids so that the addition of antioxidants is unnecessary.

Art. 19 Amendt.

Amended Claims:

1. An oral dosage form for food, food supplements and dietetics comprising perilla oil in a xylose-hardened gelatine capsule with a retarded release time.

2. The dosage from as recited in claim 1 comprising omega-3 polyunsaturated fatty acids with a high content of alpha linolenic acid.

3. The dosage form as recited in claim 1 or 2, wherein said retarded release time is more than 45 minutes.

4. The dosage form according to one of the claims 1 to 3, wherein said dosage form is operative against diseases of metabolism of fat and/or against intestinal inflammations, such as Morbus Crohn and/or colitis ulcerosa.

5. The dosage form according to one of the preceding claims, wherein the gelatine capsule comprises an ingredient selected from the group consisting of fish oil, linseed oil and gamma linolenic acid.

6. Use of a xylose-hardened gelatine capsule in order to prevent peroxidation of a polyunsaturated fatty acid contained in said gelatine capsule, wherein said gelatine capsule has a retarded release time and is used as oral dosage form for food, food supplements and dietetics.

7. The use as recited in claim 6, wherein said gelatine capsule comprises polyunsaturated fatty acids with a high content of alpha linolenic acid.

.../2

Article 19 Amendt

8. The use as recited in claim 7, wherein said gelatine capsule comprises perilla oil.

9. The use according to one of the claims 6 to 8, wherein said retarded release time is more than 45 min.

10. The use according to one of the claims 6 to 9, wherein said gelatine capsule comprises fish oil, linseed oil and gamma linolenic acid.

Abstract

Oral Dosage Form

Oral dosage form for food and food supplement as well as dietetics comprising polyunsaturated acids in a xylose-hardened gelatine capsule with a retarded release time.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
UNITED STATES RECEIVING OFFICE (RO/US)

In re Application of:	Friedel Frauendorfer
U.S. Nat'l Stage of Int'l App. No.:	PCT/EP00/03350
Int'l Filing Date:	13 April 2000
For:	ORAL DOSAGE FORM

Box PCT
ATTN: EO/US
Assistant Commissioner for Patents
Washington, D.C. 20231

Docket No.: H01.2-9587

PATENT

CORRESPONDENCE ADDRESS OF LAW FIRM

Vidas, Arrett & Steinkraus P.A. would like to make the following correspondence address of record. Please send all correspondence for this application to the address as follows:

00490
PATENT TRADEMARK OFFICE

Respectfully submitted,

VIDAS, ARRETT & STEINKRAUS

By: _____
RICHARD A. ARRETT, ESQ.
Registration No. 33,153

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Phone: (952) 563-3000
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PATENT/DESIGN PATENT

DECLARATION

As a below-named inventor, I(we) hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name;

I verily believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

ORAL DOSAGE FORM

(Insert invention title)

the specification of which is attached hereto.

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to in the declaration.

I acknowledge the duty to disclose all information which is known to be material to patentability of this application in accordance with Title 37, Code of Federal Regulations § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119, of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed.

(List prior foreign applications)

COUNTRY	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 37 USC 119
Germany	199 30 030.5	30 / 06 / 1999	[X] YES NO [ ]
			[ ] YES NO [ ]
			[ ] YES NO [ ]

I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Telephone calls and correspondence should be directed to:

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	Sole or First Inventor	**Second Inventor**
Full name:	Friedel Frauendorfer	
Inventor's signature		
Date:	29th November 2000	
Citizenship:	German	
Post office address	Gerstenstiege 24 D-30938 Großburgwedel Germany DEX	
Residence: (if different from post office address)		

(Attach additional sheets for third and subsequent inventors)